Regenerative Endodontics Versus Apexification in Immature Permanent Teeth with Apical Periodontitis: A Prospective Randomized Controlled Study

Jiacheng Lin, PhD, Qian Zeng, PhD,† Xi Wei, PhD,† Wei Zhao, PhD,* Minyi Cui, PhD,‡ Jing Gu, PhD,§ Jiaxuan Lu, PhD,* Maobin Yang, DMD, MDS, PhD,‖ and Junqi Ling, PhD¶*

Abstract

Introduction: The aim of the study was to compare the outcomes of regenerative endodontic treatment (RET) and apexification on immature permanent teeth with pulp necrosis and apical periodontitis. **Methods:** A total of 118 patients (118 teeth) were recruited and randomly assigned to either RET or apexification treatment. Each treatment group was divided into 2 subgroups according to the etiology: dens evaginatus or trauma. Clinical symptoms and complications were recorded, and cone-beam computed tomographic imaging with a limited field of view was used to measure the change of root length, root thickness, and apical foramen size at the 12-month follow-up. The *t* test/rank sum test and Fisher exact test were applied to compare the change of root morphology between RET and apexification. **Results:** One hundred three of 118 cases were completed at the 12-month follow-up. The survival rate was 100% for both treatment groups. All cases were asymptomatic with apical healing. The RET group showed a significant increase in root length and root thickness compared with the apexification group ($P < .05$). In the RET group, the cases caused by dens evaginatus achieved increased root length and root thickness compared with those caused by trauma ($P < .05$). **Conclusions:** RET and apexification achieved a comparable outcome in regard to the resolution of symptoms and apical healing. RET showed a better outcome than apexification regarding increased root thickness and root length. The etiology had an impact on the outcome of RET. Dens evaginatus cases showed better prognoses than trauma cases after RET. *(J Endod 2017;■:1–7)*

Key Words

Apexification, apical periodontitis, cone-beam computed tomography, immature teeth, regenerative endodontics

Significance

This clinical randomized controlled study compared the outcomes of RET and apexification. The results showed a high success rate of the RET group at the 12-month follow-up. Dens evaginatus cases showed better prognoses than trauma cases upon RET treatment.

Immature teeth with pulp necrosis and apical periodontitis have been a challenge for endodontic treatment because of the thin root wall and open apex. These cases are usually caused by trauma, caries, or a developmental malformation, such as dens evaginatus or dens invaginatus (1–4), resulting in pulp necrosis and arrested root development. Apexification is a conventional treatment modality for these cases in which either calcium hydroxide paste is used to induce an apical barrier or mineral trioxide aggregate (MTA) is placed as an apical barrier in order to achieve closure of the apex. Although the success rate of apexification has been reported to be between 74% and 100%, it may result in abnormal root morphology such as the formation of calcified tissue inside the root canal (5), and long-term calcium hydroxide placement may weaken the dentin and induce root fracture (6).

Regenerative endodontic treatment (RET) provides a new treatment modality for the previously described cases. In the 1960s, Dr Nygaard-Ostby (7) first raised the concept of tissue regeneration inside the root canal. In 2004, Drs Banchs and Trope (8) introduced a modified clinical regenerative endodontic protocol that involved minimal instrumentation, copious irrigation, and placement of antibiotic paste as intracanal medicament followed by inducing bleeding and the formation of a blood clot inside the root canal. In addition to a blood clot, autologous platelet-rich plasma and platelet-rich fibrin were also introduced into the root canal as alternative scaffolds because of the fact that platelet-rich plasma and platelet-rich fibrin contained molecules that could potentially induce tissue regeneration (9–11). In 2016, the American

From the *Department of Pediatric Dentistry, †Operative Dentistry and Endodontics, ‡Department of Radiology, Guanghua School of Stomatology, Affiliated Stomatological Hospital, Guangdong Provincial Key Laboratory of Stomatology, §Department of Medical Statistics and Epidemiology, School of Public Health, and ¶Guanghua School of Stomatology, Affiliated Stomatological Hospital, Guangdong Provincial Key Laboratory of Stomatology, Sun Yat-sen University, Guangzhou, Guangdong, China; and ‖Department of Endodontology, Kornberg School of Dentistry, Temple University, Philadelphia, Pennsylvania.

Address requests for reprints to Dr Junqi Ling, Affiliated Stomatological Hospital, Sun Yat-sen University, Guangzhou, Guangdong, 510055, China, or Dr Maobin Yang, Department of Endodontology, Kornberg School of Dentistry, Temple University, Philadelphia, PA 19140. E-mail address: lingjq@mail.sysu.edu.cn or myang@temple.edu

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TABLE 1. Cases Recruited in the Regenerative Endodontic Treatment (RET) and Apexification Groups

Tooth types	RET			Apexification			
	Premolar	Central incisor		Premolar	Central incisor		
Etiology	Dens evaginatus	Trauma	Total	Dens evaginatus	Trauma	Total	Total
Original case (*n*)	53	27	80	23	15	38	118
Lost case (*n*)	5	6	11	2	2	4	15
Final case (*n*) (12-month follow-up)	48	21	69	21	13	34	103

Association of Endodontists proposed a standard protocol for regenerative endodontic procedures (12). To date, numerous case reports and cases series showed "success" of RET, which was defined as the disappearance of the periapical lesion and continued root development.

Comparison of the success rate between apexification and RET has been reported in several retrospective and prospective studies (13–18) although the result is still inconclusive because of the variable study designs and limited sample numbers. A clinical randomized study with a larger size of samples is needed. In some RET cases, complications such as external root resorption and discoloration were noticed but never systematically analyzed (14). The aim of this study was to compare the outcomes of RET and apexification on immature permanent teeth with pulp necrosis and apical periodontitis.

Materials and Methods

Patient Recruitment and Randomization

This study was approved by the Ethics Committee of the Affiliated Hospital of Stomatology, Sun Yat-sen University, Guangzhou, Guangdong, China, and registered in ClinicalTrials.gov (ID: NCT01799187). Patients were recruited from the Department of Pediatric Dentistry of the dental hospital from June 2013 to May 2015. The inclusion criteria were as follows: patients between 6 and 18 years old; pulp necrosis, which was defined by a negative response to the temperature test and the electric pulp test; radiographic evidence of immature teeth with a single canal, open apices larger than 1 mm in diameter, and presence of periapical radiolucency; and the involved tooth had either dens evaginatus or a history of trauma. The exclusion criteria were patients with chronic systematic disease, patients allergic to the antibiotics used in the study, a vital tooth, a tooth with periodontal disease, a tooth with more than 1 canal, and radiographic evidence of a root fracture. Envelopes containing information on RET or apexification were prepared with a ratio of 2 to 1 and randomly assigned to the patients. All the clinical procedures were performed by 1 experienced endodontist who also had special training in pediatric dentistry.

Regenerative Endodontic Procedure

After local anesthesia with 2% lidocaine (no epinephrine [Lidocaine Hydrochloride Injection; Hubei Tiansheng Kangdi Pharmaceutical Co Ltd, Hubei Sheng, China]), the tooth was isolated with a rubber dam, and access was performed with a #4 round bur. The canal was then irrigated with 20 mL 1.5% sodium hypochlorite solution (Tanxiao Fengwei Pharmaceutical Co Ltd, Guangdong Province, China), 0.9% physiological saline, and 20 mL 17% EDTA (Zhongnan Reagent Industry Co Ltd, Hunan Province, China). The canal was dried with a paper point, and 0.1 mg/mL triple antibiotic paste was delivered into the canal with a Lentulo spiral in which ciprofloxacin (Sigma-Aldrich, St Louis, MO), metronidazole (Sigma-Aldrich), and clindamycin hydrochloride (Sigma-Aldrich) were equally mixed with distilled water. The tooth was temporarily sealed with Caviton (GC Corporation, Tokyo, Japan).

After 3 weeks, patients presented for the second visit. If the symptom was not relieved, root canals were remedicated with triple antibiotic paste for another 3 weeks. The asymptomatic tooth proceeded to the next step of RET treatment. After local anesthesia with 2% lidocaine (no epinephrine) and rubber dam isolation, the tooth was reaccessed. The triple antibiotic paste was removed with 0.9% saline, and 20 mL 17% EDTA solution was applied to the canal; after this, the canal was dried with paper points. Bleeding was induced by overinstrumenting with a #25 file and allowed to reach 3–4 mm below the cementoenamel junction (CEJ) to form a blood clot. An absorbable collagen barrier (Heal-all Biological Membrane; Zhenghai Biological Technology Co Ltd, Shandong Province, China) was placed on top of the blood clot followed with white MTA (ProRoot MTA White; Dentsply International, Inc, Konstanz, Germany). Then, the tooth was sealed with glass ionomer cement (GlasIonomer FX-II; Shofu Inc, Kyoto, Japan). After 7 days, the glass ionomer cement was removed, and the set of MTA was confirmed. The tooth was finally restored with composite resin (Z350; 3M ESPE, St Paul, MN).

Apexification Procedure

Local anesthesia was performed with 2% lidocaine. The tooth was isolated with a rubber dam, and pulp access was performed. The canal was irrigated with 20 mL 1.5% sodium hypochlorite and 0.9% physiological saline followed by 20 mL 17% EDTA. After being dried with paper points, calcium hydroxide paste was placed into the canal, and the tooth was temporarily sealed with Caviton.

One week later, the tooth was reaccessed after isolation with a rubber dam. Calcium hydroxide paste was removed using 17% EDTA irrigation. The root canal was dried with paper points, and Vitapex paste (Neo Dental International, Inc, Tokyo, Japan) was injected into the canal before the tooth was sealed with glass ionomer cement. During the

TABLE 2. Baseline of the Root Morphology Measured by Cone-beam Computed Tomographic Imaging (Preoperative)

Indexes (mm)	RET (*n* = 69)	Apexification (*n* = 34)	*P* value*
Size of apical foramen	2.11 ± 0.86	2.02 ± 0.82	.882
Root length	11.60 ± 1.17	11.39 ± 1.69	.912
Root thickness	1.41 ± 0.02	1.43 ± 0.04	.962

*The *t* test/rank sum test.